Cancer Medicine Journal

Research Article | Vol 7 Issue 2

Effect of Exposure to Ambient Air Pollution on Gynecological Cancer: A Systematic Review

Rachael Gakii Murithi* **and Chan Lu**

Department of Occupational and Environmental Health, XiangYa School of Public Health, Central South University, Changsha, China

Correspondence should be addressed to Rachael Gakii Murithi, Department of Occupational and Environmental Health, XiangYa School of Public Health, Central South University, Changsha, China

Received: July 30, 2024; Accepted: August 25, 2024; Published: August 31, 2024

ABSTRACT

BACKGROUND

The importance of gynecological cancer and air pollution awareness cannot be overemphasized. Various studies undertaken worldwide have found that exposure to atmospheric pollutants can lead to high morbidity and mortality due to gynecological cancer. Hence, it is critical to address this issue for the prevention and reduction of gynecological cancers.

OBJECTIVE

This review was conducted to objectively assess the effect of exposure to ambient air pollution on gynecological cancer and its related factors among women.

METHODS

A systematic review and meta-analysis of quantitative research were conducted. We searched 5 electronic databases: CINAHL (EBSCO Academic Search Premier); Google Scholar; Embase; PubMed and Web of Knowledge to identify relevant studies for inclusion from January 2011 to December 2021. The quality of each study included for the meta-analysis was determined using the Joanna Briggs Institute Critical appraisal tool.

RESULTS

18,324 records were identified from the electronic data search. 16,535 records were filtered systematically. Finally, 12 studies involving 5 population-based cross-sectional studies using secondary data from demographic health surveys conducted prior, 2 cohort studies, 3 articles are case-control studies, 1 ecological study, and 1 meta-analysis were added in the final analysis. Accordingly, the overall point estimate of gynecological (cervical, ovarian, and endometrial) cancer among women worldwide was 50% (95%CI: 43%~57%). High heterogeneity (I_2 = 99.72%, p <0.001) was noticed which could be due to factors not explored in this review. The factors commonly associated with gynecological cancer were occupation, procreation, age, diabetes, the number of births, drinking, a family history of cancer, menstrual cycle, and environmental tobacco smoke (ETS).

Citation: Rachael Gakii Murithi, Effect of Exposure to Ambient Air Pollution on Gynecological Cancer: A Systematic Review. Int J Can Med J 7(2): 63-81.

CONCLUSION

Long-term air pollution exposure has a significant impact on the occurrence and development of gynecological tumors. The interaction between ambient air pollution and sensitive determinants can significantly increase the risk of gynecological tumors. Air pollution exposure may be high in most countries worldwide. Hence, there was heterogeneity in the effect of exposure to ambient air pollution on gynecological cancer.

KEYWORDS

Gynecological cancers; Ambient air pollution; Temperature; Diurnal temperature variation; Interaction effect

INRODUCTION

Cancer is one of the most serious and horrible diseases in the world. In 2015, the World Health Organization estimated that in 91 countries around the world, cancer was the first or second cause of death before the age of 70 [1]. Cancer is a global problem demanding a global solution. According to statistics, the annual cancer burden in the world is estimated to be about 18 million cases, with more than 9 million deaths [2]. In 2017, over a million women were diagnosed with malignant gynecological (endometrial, cervical, and ovarian) tumors [3]. Gynecological cancers (GC) are the leading heavy cancer burden for women, with high morbidity and mortality [4]. Gynecological cancers account for 16% of all diagnosed malignancies in women, translating to over a million cases globally [5]. Gynecological cancers are the leading heavy cancer burden for women, with high morbidity and mortality [6]. Endometrial, ovarian, and cervical cancers are the most occurring tumors in women [7,8]. Gynecological neoplasm in women causes high morbidity and mortality [9], which leads to a heavy burden for women [6]. The World Health Organization (WHO) ranked cervical tumors as the eighth-most common of all human cancers [10]. In 2019, the
global incidence of and mortality from corpus uteri were reported to be very high [11]. Ovarian tumors have reported the third-highest death toll [12].

The World Health Organization (WHO) reported that the global incidence and mortality from corpus uteri in 2018 were 382,069 and 89,929, respectively [10]. The treatment of gynecological cancer usually includes surgery, chemotherapy and radiotherapy. On the one hand, these treatments will increase the economic burden of families, on the other hand, they will seriously affect the quality of life of women and families. Related studies have shown that chemotherapy drugs and some treatments may also lead to severe health damage [13]. Because gynecological cancer has such a serious impact on people, it is necessary to make an in-depth study on its influencing factors.

China has reported high gynecological malignancies incidence among the elderly population [14]. Women with gynecological cancers are more likely to suffer from physiological and psychological problems, such as losing fertility [15-17] and having sexual dysfunction [18-20] and becoming anxiety and depression [21-23]. Hence, urgent investigations on determinants for gynecological cancers are required for its reduction and prevention. Air pollution is an issue [24, 25] that impacts health [26]. Detailed exploration is required on how air pollutants affect health [27]. Recently, reported gynecological cases have been on the rise in China and other industrialized nations [28-30]. Therefore, our study aimed to explore the correlations between the short-and long-term exposure to ambient air pollutants (SO_2, NO_2, and PM_{10}) and gynecological tumors.

Air pollution is an important influencing factor related to gynecological tumors. Previous studies show that air pollutants exposure is considered to be linked to an

increase in the risk of health disorders in women. Besides, pollutant's high concentrations increase the risk of gynecological cancer [31]. Multiple studies support the relationship between polycyclic aromatic hydrocarbons and ovarian cancer [32], cervical epithelial tumor [33], uterine dysplasia [34], breast cancer [35], reproductive dysfunction, and pathological changes [36]. Many previous research has not touched on the interrelations between air pollutants (SO_2, NO_2, and other pollutants) and ovarian tumor [32,37], and cervical tumor [38] mortality, demanding further investigations on the link between tumor etiology and air pollutants.

More and more evidence suggesting that air pollution can influence human health, including a broad range of acute and chronic diseases [39-42] as well as specific cancers, such as breast cancer [43], lung cancer [44], bladder cancer, kidney cancer and colorectal cancer [45], brain cancer [46], laryngeal cancer [47], gastric cancer [48] and Childhood Leukemia [49]. However, minimal research has examined a possible interaction between ambient air pollution exposure and gynecological cancer in the general population. Previous studies showed associations between cervical cancer and diesel engine exhaust [50]. A study confirmed positive relations between diesel exhaust and ovarian cancer [51]. Some recent studies also found that PM2.5 was significantly associated with ovarian cancer [32,52]. Thus, it is essential to address the effect of exposure to air pollutants on gynecological cancer, especially with ubiquitous air pollution.

Most of the research on the risk factors of gynecological tumors focus on a single tumor. In addition, there are few studies on the correlation between air pollutants and cervical cancer and endometrial cancer; as well as the relationship between pollutants and gynecological tumors in the previous studies, and most of them studied the short-term exposure to pollutants, and only a few studied the correlation between long-term exposure of pollutants and gynecological tumors [8]. Furthermore, Previous studies mainly studied the correlation between air pollution and tumors in western countries. As a developing country, the composition of air pollutants in China is not similar to that in western countries. In view of this, it is necessary to determine the correlation between long-term exposure of pollutants and gynecological tumors, and the relationship between pollutants and gynecological tumors in developing countries.

Meteorological factors are another important influencing factor of cancer. Temperature is the most important meteorological parameter. A study in the United States shows that cold ambient temperature may be a potential carcinogenic factor. People living in cold environments may have a higher risk of cancer and death. External body temperature may have a significant impact on changing cell metabolism, leading to cancer [53]. Epidemiological research recently deduced that outdoor diurnal temperature variation (DTV) daily temperature changes affect health [54,55]. Therefore, it is speculated that average temperature and DTV may influence the occurrence of gynecological tumors. Moreover, previous studies on the correlation between temperature and cancer focused on short-term exposure, while studies on the effects of long-term temperature exposure were very few so it is necessary to study the link between gynecological tumor and long-term temperature changes.

There are very few publications on the correlation between pollutants/temperature and gynecological tumors, and even fewer studies have been done on the interaction between pollutants and temperature. Air pollution in developing countries, especially China, is becoming more and more serious, and climate change is intensifying. The interaction between the two has a serious impact on human health. We hypothesized that ambient air pollution exposure (PM_{10}, SO_2, and NO_2) was correlated with gynecological (endometrial, ovarian, and cervical) tumor. To verify this

hypothesis, we conducted a systematic review to establish possible correlations between ambient air pollutants (PM_{10}, NO_2, and SO_2) and gynecological tumors with exposure assessment of broad coordination of potential confounders, such as family history of cancer, age, occupation, number of births, menstrual cycle, ETS, drinking, and diabetes. In this study, we systematically evaluated the correlation between gynecological (ovarian, endometrial, and cervical) cancer and air pollutants NO_2, SO_2, and PM_{10}.

METHODOLOGY

Search Strategy

This meta-analysis and systematic review were conducted to assess the effect of exposure to ambient air pollution on gynecological cancer. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 guideline was used in screening eligibility for the studies. The databases used to search for studies were: CINAHL, EMBASE, PUBMED, and Web of Science. An additional search was done with Google Scholar as supplementary. The search terms used included: "NO_2, SO_2, PM_{10}, ambient air pollution, temperature exposure, long-term exposure, gynecological cancer, short-term exposure". Boolean operators like; 'AND' and 'OR' were used, alongside phrase searching, proximity operator, and truncation. Through this process, a Search Strategy was generated for each individual database. Search strategy such as: ((((((((((Environmental pollution) OR (temperature)) OR (Gynecological tumors)) AND (Ambient air pollution)) OR (gynecological cancer)) was used in PubMed and TS = (prevention or reduction or interaction) AND TS = (prevention) AND TS = (reduction) AND TS = (interaction) for Web of Science.

A systematic review of published literature was carried out from the 5th October to 30th October 2021 and included studies published in the last 10 years (2011 to 2021).

Study Selection and Eligibility Criteria

The selected articles were independently screened using the titles and abstracts before retrieving full-text articles from two investigators (KVJ & XJ). Certain specific criteria were used to screen the full-text papers that were used further. The selection of the final paper included a third reviewer, and the decision was made after discussing the disagreements and coming to a consensus.

All studies that reported the total effect of short-term and/or long-term exposure to ambient air pollution on gynecological (ovarian, endometrial, and cervical) cancer were included in the meta-analysis and literature review. We analyzed the effect of exposure to ambient air pollution (PM_{10}, SO_2, and NO_2) on gynecological (ovarian, endometrial, and cervical) cancer. Hence, the final analysis was performed according to gynecological cancer cases.

The review included studies between 2011 and 2021 and all publications such as cross-sectional, case-control, and cohort studies that had a population-based design and reported the effect of exposure to ambient air pollution (PM_{10}, SO_2, and NO_2) on gynecological (ovarian, endometrial, and cervical) cancer. The outcome of the study was the effect of exposure to ambient air pollution on gynecological cancer, and its risk factors among the women population. Factors reported by studies such as age, occupation, number of births, menstrual cycle, diabetes, family history of cancer, environmental tobacco smoke (ETS), and drinking were considered as factors associated with gynecological cancer. EndNote reference manager was used to keep track of all generated references. Articles written in English only were eligible for inclusion and references to the selected articles were screened for inclusion in the review.

This review excluded articles with measures other than the WHO recommendation for gynecological (ovarian, endometrial, and cervical) cancer. The review also excluded articles with titles that did not address

gynecological (ovarian, endometrial, and cervical) cancer and also articles that did not report on factors associated with ambient air pollution exposure and gynecological (ovarian, endometrial, and cervical) cancer. Case reports and qualitative studies were also excluded from the review.

Data Extraction

To minimize the likelihood of errors going unseen, two investigators performed data extraction independently (KVJ & XJ) and their results were compared. A standard data extraction form was used by both data extractors.

A standardized form with the following domains: first author's name, year of publication, country, cancer type (ovarian, endometrial, or cervical cancer), year of study, study design, sample size/study population, age range, pollutant, and exposure duration, was used to extract the information for each paper (Table 1).

Authors & year	Country	Cancer Type	Year	Study Design	SS	Age Range	Pollutant	Exposure Duration
Adegoke et al. 2012 [65]	United States (USA)	Cervical	1973-2007	Cohort	37,776	20-85	-	High
Villanueva et al. 2021 [60]	California, USA	Ovarian	1996-2014	Case-Control	5,074	25-29	SO_2, $PM_{2.5}$	High
Yu et al. 2021 [31]	Beijing, China	Gynecological	Dec 2008 to Dec 2017	Case-Control	10,502	25-95	$PM_{2.5}$, CO, O_3, and SO_2	High
Xu et al.2021 [59]	Changsha, China	Cervical, Ovarian, Endometrial	June 2010 to Dec 2018	Case-Control	704	10-90	SO_2	High
Matz et al. 2017 [67]	60 countries	Ovarian	1995-2009	Population-based Study	6,95,932	15-99	-	High
Al-Ahmadi a. 2013 [64]	Saudi Arabia	Cervical, Ovarian	Jan 1998 to Dec 2004	Cohort	45,532	-	NO_2	High
Ayuso Álvarez et al. 2020 [61]	Spain	Ovarian	1999-2008	Ecological Study	8,073 Spanish towns	0-85+	H2S, PM_{10}, SOx, NO_2	High
Bray et al. 2018 [1]	Worldwide	Cervical	2018	Population-based Study 2018 Data	5,70,000	0-85+	-	High
Hung et al. 2012a [32]	Taiwan	Ovarian	2006-2009	Population-based Study	61 municipalities	-	$PM_{2.5}$	High
Lai et al. 2017 [66]	Taiwan	Endometrial	1991-2010	Population-based Registry Study	15,542	25-85+	-	High
Shi et al. 2012 [62]	China	Cervical	1973-1975, 1990-1992, 2004-2005	Meta-Analysis	29, 27 and 31 provinces	0-65	-	High
Wu et al. 2018 [63]	United States	Ovarian	1983-2012	Population-based Study	18 states	20-70	-	High

Table 1: Characteristics of studies included in a systematic review of ambient air pollution and gynecological cancer in women (n = 12).

Quality Assessment of Included Articles

The quality of the included studies was assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist [56]. The tool consists of 9 questions assessing different aspects including but not limited to sample representativeness of the target population, adequacy of sample size, participants recruitment process, detailed description of the study setting and subjects, sufficient coverage of the data analysis, objective criteria in the measurement of the outcome variable(s) and identification of the sub-population, reliability, appropriateness statistical analysis and identification of confounding variables. To appraise a study, each question is scored as Yes (✓) if it has a high quality or No (X) if it has the low

or medium quality, and others are unclear and not applicable after which a score is allocated to each study. The quality assessment scores of each article or study are summarized (Table 2).

	1	2	3	4	5	6	7	8	9	Overall
Adegoke et al. 2012 [65]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Villanueva et al. 2021 [60]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Yu et al. 2021 [31]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Xu et al. 2021 [59]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Matz et al. 2017 [67]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Al-Ahmadi a. 2013 [64]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Ayuso Álvarez et al. 2020 [61]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Bray et al. 2018 [1]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Hung et al. 2012 32]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Lai et al. 2017 [66]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High
Shi et al. 2012 [62]	✓	✓	✓	✓	✓	✓	✓	✓	NA	High
Wu et al. 2018 [63]	✓	✓	✓	✓	✓	✓	✓	✓	✓	High

Table 2: Quality assessment of included articles using JBI appraisal.

Note: Yes = ✓; No = X; Unclear = UC and Not applicable = NA.; 1 = was the sample frame appropriate to address the target population? ; 2= were study participants recruited in an appropriate way?; 3 = was the sample size adequate?; 4 = were the study subjects and setting described in detail?; 5 = was data analysis conducted with sufficient coverage of the identified sample?; 6 = were valid methods used for the identification of the condition?; 7 = was the condition measured in a standard, reliable way for all participants?; 8 = was there appropriate statistical analysis?; 9 = was the response rate adequate, and if not, was the low response rate managed appropriately?

Statistical Analysis and Data Synthesis

We conducted a meta-analysis to obtain a pooled prevalence rate and 95% CI using Stata Corp version 16. The heterogeneity of the analyzed studies was examined using I2 statistic (Heterogeneity is usually quantified by the I2 statistic and formally tested by Cochran's Q test.). The interpretation of the I2 value was as follows <25%, low heterogeneity; 25%-75%, moderate heterogeneity; and >75%, high heterogeneity [57]. To calculate the pooled prevalence rates, fixed effect or random effect models were used if heterogeneity was low or moderate to high respectively [58]. Subgroup analysis was conducted based on the category of gynecological cancer that the participants were diagnosed with. Therefore, studies were grouped based on the above category, and a pooled prevalence was generated. The factors associated with gynecological cancer were examined using confidence intervals and odds ratios.

RESULTS

Search Results

The electronic search yielded a total of 18,324 articles including Google Scholar and through manual search of the reference list of selected articles. A total of 1,689 were removed as duplicates leaving a balance of 16,635 articles. After the removal of the duplicates, the titles and abstracts of 16,635 articles were scanned. A total of 16,535 articles were removed after the scanning of the titles, and abstracts and considering the exclusion criteria. Therefore, a balance of 100 full-text articles were screened by applying the inclusion criteria and other parameters that are not compatible with the review objectives as shown in Figure 1. Quality assessment of the retrieved articles using the PRISMA guidelines resulted in the exclusion of 88 articles. Therefore, the final analysis included 12 studies.

Study Characteristics

Table 2 provides the characteristics of included studies in this meta-analysis and systematic review. The majority of the studies (90.5%) used cross-sectional design and were published between 2011 and 2021. A total sample size of over 1 million women from the twelve studies was used in the meta-analysis and systemic review and the range of the sample size was from 704 to over 600,000 participants. A total of 5 population-based cross-sectional studies using secondary data from demographic health surveys were conducted prior, 2 cohort studies, 3 articles are case-control

studies, 1 ecological study, and 1 meta-analysis were included in the final analysis. In the review, the majority of the studies were from China (n = 5) followed by the USA with 3 articles.

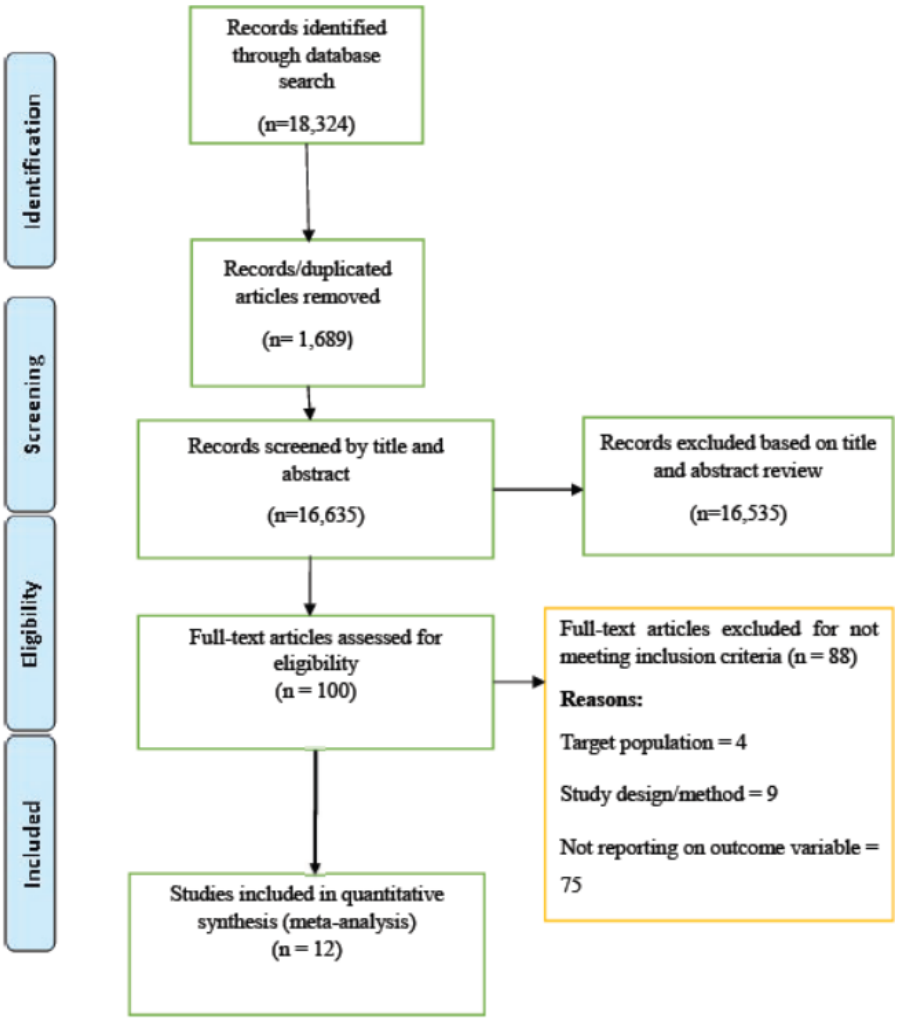

Figure 1: Flow diagram of the screening and selection process used in the review.

The prevalence or participation rate ranged from 12% to 83% and the common atmospheric pollutants associated with gynecological cancer are NO_2, SO_2, $PM_{2.5}$, O_3, CO, and organic chemicals (Table 3). Sub-regionally, the studies that were included are from America (n = 3), Europe (n = 1), Asia (n = 6), and other parts of the world (n = 2). All the 12 studies were deemed high quality as they fulfill 8 of the 9 criteria per the JBI checklist (Table 2).

Authors	NO2; OR (95% CI)	SO2; OR (95% CI)	PM2.5; OR (95% CI)	Ozone O3; OR (95% CI)	CO; OR (95% CI)	Organic Chemicals; OR (95% CI)
Villanueva et al. 2021 [60]	1.30(1.25–1.36)	-	1.45(1.41–1.49)	-	-	-
Yu et al. 2021 [31]	-	1.015(1.008–1.021)	1.004(1.003–1.006)	1.002(1.000–1.005)	1.120(0.993–1.246)	-
Xu et al. 2021 [59]	-	1.56(1.10–2.21)	-	-	-	-
Ayuso-Álvarez et al. 2020 [61]	-	-	-	-	-	1.10(1.02–1.20)
Hung et al. 2012 [32]	-	-	1.2(1.02–1.41)	-	-	-

Table 3: Common air pollutants associated with gynecological (cervical, ovarian, endometrial) cancer in women.

Subgroup Analyses

Subgroup analysis was done for the China region and the gynecological cancer type variance. Results of the subgroup analysis as shown in Table 4 showed the epidemiology of gynecological cancer in China and high between-study variability. This high heterogeneity could have resulted from the difference in sample size and also the study designs of the included studies.

China Region	ASIR (per 100,000)	AAPC	APC	ASMR (per 100,000)	Mortality Rate Peak (Age)	Survival Rates (Overall)
Cervical Cancer	10.3	7.10%	6.80%	2.6	85+	45.40%
Endometrial Cancer	6.33	3.40%	3.70%	2.7	55–59	55.10%
Ovarian Cancer	5.32	4.50%	4.50%	3.21	75–79	38.90%
Overall	201.1	-	-	126.9	-	-

Table 4: Subgroup analysis for comparison of the different gynecological cancers' epidemiology characteristics. **Note:** ASIR: Age-Standardized Incidence Rate; AAPC: Average Annual Percentage Change; APC: Annual Percentage Change; ASMR: Age-Standardized Mortality Rate.

Gynecological Cancer Epidemiology

As seen in Table 3, the results showed that the overall ASIR and ASMR of gynecological cancer among women in the China region were 201.1 and 126.9 per 100,000, respectively. The overall survival rates for cervical, endometrial, and ovarian cancer were 45.4%, 55.1%, and 38.9% respectively. This showed that the burden of gynecological cancer is high in China.

Factors Associated with Gynecological Cancer

This review discusses relevant primary research articles, cohort studies, reviews, meta-analyses, and population-based studies on gynecological cancer, summarizing the negative and positive gynecologic cancer risk determinants. PubMed and other search engines were used. There was discussions for confounding determinants under separate analysis including, personal factors (age, occupation, number of births, menstrual cycle), disease history (diabetes, family history of cancer), as well as living habits (environmental tobacco smoke (ETS), drinking).

Sociodemographic Characteristics

In this review, the sociodemographic factors assessed in the analysis are occupation, age, the number of births, procreation, family history of cancer, environmental tobacco smoke (ETS), diabetes, menstrual cycle, and drinking. For each of the variables associated with gynecological cancer, a separate analysis was conducted.

Seven articles were incorporated to assess the relationship between age and gynecological cancer [32,60-65]. All the seven studies included found significant associations between age and gynecological cancer risk. The final pooled meta-analysis found that women of child-bearing age were more susceptible to the risk of gynecological cancer due to air pollution.

Six articles [60-65] were incorporated to assess the relationship between occupation/SES and gynecological cancer. All the six studies included showed significant associations between occupation/SES and gynecological cancer risk. The final pooled meta-analysis found that wealthier women (those who can live on a paycheck) or women from wealthy families were more susceptible to the risk of gynecological cancer due to air pollution.

Four articles [60,64,66,67] were incorporated to assess the relationship between procreation and gynecological cancer. All four studies included showed significant associations between procreation and gynecological cancer risk. The final pooled meta-analysis found that women who

had given birth (procreation) were more susceptible to the gynecological cancer risk due to air pollution.

Two articles [60,66] were incorporated to assess the relationship between the number of births and gynecological cancer. The two studies included showed significant associations between the number of births and gynecological cancer risk. The final pooled meta-analysis found that women who had given birth to more children were more susceptible to the risk of gynecological cancer due to air pollution.

One article [68] was incorporated to assess the relationship between diabetes and gynecological cancer. The included study showed significant associations between diabetes and gynecological cancer risk. The final pooled meta-analysis found that women who had a personal history of diabetes were more susceptible to the risk of gynecological cancer due to air pollution.

Three articles [61,69,70] were incorporated to assess the interaction between gynecological cancer and family history of cancer. The three included studies showed significant associations between family history of cancer and gynecological cancer risk. However, the final pooled meta-analysis using data from the three articles showed that women with a family history of cancer were more susceptible to the risk of gynecological cancer due to air pollution.

Three articles [60,63,66] were incorporated to assess the relationship between smoking and gynecological cancer. The three included studies showed significant associations between direct smoking and gynecological cancer risk. However, no positive associations were found on ETS. The final pooled meta-analysis found that women involved in smoking were more susceptible to the risk of gynecological cancer due to air pollution.

Two articles [60,69] were incorporated to assess the relationship between drinking and gynecological cancer. The two included studies showed significant associations between drinking and gynecological cancer risk. The final pooled meta-analysis found that women who take alcoholic drinks and beverages were more susceptible to the risk of gynecological cancer due to air pollution.

One article [60] was also incorporated to determine the relationship between the menstrual cycle and gynecological cancer. The included study showed positive associations between the menstrual cycle and gynecological cancer risk. The final pooled meta-analysis found that women of reproductive age were more susceptible to the risk of gynecological cancer due to air pollution.

There was high heterogeneity in five of the nine factors included in the analysis for meta-analysis.

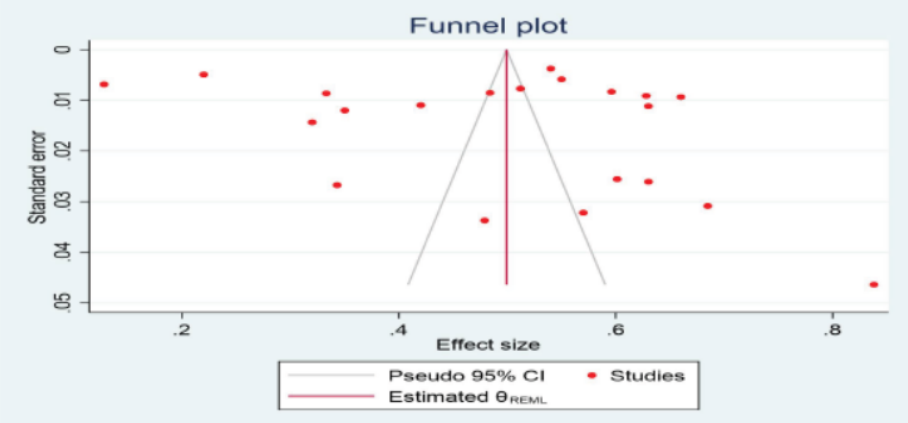

Figure 2: Funnel plot predicting publication bias.

Publication Bias

Publication bias was checked for the studies that were analyzed in the meta-analysis, although it was not very applicable in this situation because Begg's and Egger's tests was not suitable for this study. This was a result of the interrelation between effect size and its standard error. The result of effect estimates against standard error showed publication bias with a p-value of 0.001, by using a nonparametric trim-and-fill analysis of the publication bias method (Figure 2).

DISCUSSION

Ambient Air Pollution and Gynecological Cancer Relationship

To our best knowledge, we believed this systematic review and meta-analysis is the first on the effect of exposure to ambient air pollution on gynecological cancer. The review was not limited to China only in order to increase heterogeneity between studies and also due to the limited studies on ambient pollution and gynecological cancer across the globe. We obtained this report from the analysis of data collected through a systematic review of scientific publications on gynecological cancer between January 2011 and December 2021. The literature was very diverse and contained different sample sizes, study designs, sampling techniques, and data collection methods. In addition six of the included articles used secondary data (demographic Health Survey).

In the studies that were included, we found that sociodemographic factors were among the most frequently studied factors commonly associated with gynecological cancer. The low number of gynecological studies was one gap that was significantly identified in this review. The age of the women that participated in the studies ranged from the of age 20 years and above, subjecting to recall bias. However, 12 studies were used for the final meta-analyses and systematic review.

The major findings from our review analysis are discussed below and include reported experiences on the factors associated with the effect of exposure to ambient air pollution and gynecological cancer. Despite the meticulousness and rigor, we found that the magnitude of the effect of short- and long-term exposure to ambient air pollution on gynecological cancer was high. The higher adjusted ORs of gynecological cancer risk were found to be linked to the increased concentrations of each pollutant (PM_{10}, $PM_{2.5}$, CO, O_3, SOx, H2S, SO_2, and NO_2). Identification of the nonlinear association between the gynecological cancer risk and the women's exposure to air pollutants (SO_2, PM_{10}, and NO_2) was identified using the ORs calculated for the different levels of air pollutants. By nature of the included articles, the majority are within the areas of China, as it is the most notorious for air pollution. Hence, gynecological cancer risk due to exposure to ambient air pollutants can be linked to many factors.

Although these factors are discussed separately, they are not mutually exclusive. Hence, they all sum up report of the major areas identified in our findings. Based on the sample source of our study, we were able to detect in our subgroup analysis that both the studies with qualitative design and those with quantitative cross-sectional design indicated higher effects. While the heterogeneity still remains high in each case, the qualitative design seems to be optimal in predicting ambient air pollution exposure effects on gynecological cancer. Understanding individual and environmental factors associated with gynecological cancer risk will help to design appropriate strategies and policies for improving gynecological health service utilization.

In our review, the women's age was a factor associated with the effect of exposure to ambient air pollution exposure effect on gynecological cancer risk. The age of women was significantly associated with gynecological

cancer, in that, older women were more susceptible to gynecological cancer risk due to ambient air pollution exposure than younger women. Overall, according to the studies' analyses, gynecological cancer incidence was found to be highest in women aged between 40 years and 49 years. The women's occupation or SES was a factor associated with the effect of exposure to ambient air pollution on gynecological cancer risk. These studies' analyses found that women who had an occupation or were employed (high SES) were more susceptible to gynecological cancer risk due to the air pollutants effect. Procreation and the number of births were factors associated with the effect of exposure to ambient air pollution on gynecological cancer risk.

The studies analyses found that women who had given birth and had more children were more susceptible to gynecological cancer risk due to long-term exposure to ambient air pollution. Personal or family history of cancer and diabetes was a factor associated with the effect of exposure to ambient air pollution on gynecological cancer risk. Some studies analyses found that women with no family history of cancer were more susceptible to gynecological cancer risk due to long-term exposure to ambient air pollution. Others found that diabetes and a family history of cancer made the women more susceptible to the risk of the disease. Environmental tobacco smoke and personal factors such as drinking and menstrual cycle were also factors potentially associated with the effect of exposure to ambient air pollution on gynecological cancer risk.

The overall magnitude of the effect of exposure to ambient air pollution on gynecological cancer risk was shown to be high by the subgroup analyses. The prevalence of gynecological cancer by region displayed a higher pooled estimates of gynecological cancer cases in Asia followed by Europe, America, and Africa [71] according to a subgroup meta-analysis. While extrapolating the magnitude of lower prevalence and incidence of gynecological cancer in countries, slow industrialization could be a factor. Apparently, in addition to awareness, accessibility to gynecological cancer screening service visits is a key factor. The regions faced with civil unrest and high crime rates where women and children are the most vulnerable, it is indeed normal to register low gynecological cancer screening service visits. In addition, SES is still a major determinant in Chinese women's participation in regular gynecological cancer screening check-ups.

Studies conducted in the USA [31,64], China [60,62,64], Taiwan [59,69], and Spain [63] showed significant associations between age and the risk of gynecological (cervical, ovarian, endometrial) cancer due to air pollution exposure. These studies revealed that older women had higher odds of the risk of gynecological cancer due to air pollution exposure than younger women. According to recent data findings on the epidemiology of gynecologic cancers in China [72], the ASIR for cervical cancer, endometrial cancer, and ovarian cancer was found to be 10.3, 6.33, and 5.32, respectively, per 100,000 women. The ASMR for cervical cancer, endometrial cancer, and ovarian cancer was found to be 2.6, 2.70, and 3.21, respectively, per 100,000 women. The mortality peak (age) for cervical cancer, endometrial cancer, and ovarian cancer was 85+, 55 years - 59 years, and 75 years - 79 years, respectively.

Studies conducted globally [66] showed significant associations between occupation/SES and the risk of gynecological cancer risk due to air pollution exposure. These studies revealed that women with low SES had higher odds of the risk of gynecological cancer due to air pollution exposure than women with high SES. Studies conducted in China revealed that women with lower SES had higher odds of gynecological (cervical, ovarian, endometrial) cancer risk due to exposure to industrial

pollutant SO_2 [60,62]. Studies done in the United States [61,65,73] found that low SES was a risk factor for ovarian cancer. Studies done in Saudi Arabia [67] also associated low SES to both ovarian and cervical cancer. Generally, women with low SES are likely to be living in poor housing and high environmental pollution residential areas. Other studies have demonstrated that cervical cancer is recurrent in women in the lower SES group [74,75]. Moreover, China's cervical cancer morbidity was recently reported to be comparatively low at the registration place in a region with a higher SES [64,65]. High SES could enable a better level of medical care, providing early diagnosis, detection, and treatment for the disease. However, other studies showed that cancer risk and community exposure to pollution at the workplace are crucial environmental health issues [76,77].

Studies conducted in the United States [67], China [61,64], and globally [66] showed significant associations between procreation and gynecological cancer risk resulting from air pollution exposure. These studies revealed that women who had given birth had higher odds of gynecological cancer risk resulting from air pollution exposure than women who had never given birth. Other studies [60,66] further showed significant associations between the number of births and gynecological cancer risk due to exposure to air pollution. These studies revealed that women who had given birth to more children had more odds of gynecological cancer risk due to exposure to air pollution than women who had never given birth.

A recent study conducted in Taiwan [69] showed significant associations between diabetes and gynecological cancer risk. This study revealed that women who had diabetes had more odds of gynecological (endometrial) cancer risk than women who had no diabetes or personal history of diabetes. Other studies conducted in China [60], Taiwan [69], and other 60 countries [70] showed the interrelations between family history of cancer and gynecological cancer risk. These studies [69,70] revealed that women who had a family history of cancer were more susceptible to gynecological cancer risk than women who had no personal or family history of cancer. However, in contrast, one of the studies [60] showed that women without a family history of cancer were more susceptible to gynecological (cervical, ovarian, endometrial) cancer risk due to long-term exposure to SO_2. Heredity may also affect how air pollution exposure interconnects with cancer. According to Boyle et al., the increasing aging female population would increase cancer incidents globally [76].

A recent study done in China [60] showed no significant associations between smoking/ETS, drinking, menstruation cycle, and the risk of gynecological cancer due to air pollutants exposure. However, one study in Taiwan [69] showed significant associations between drinking and endometrial cancer risk. This study revealed that women who drink alcohol had higher odds of endometrial cancer risk than women who do not drink alcohol. With regards to the menstruation cycle, the periodic secretions, proliferation, shedding, and hormonal changes in women may be linked to gynecological tumors [60]. However, further investigation is required.

This suggests that the women’s occupation status, procreation status, age, the number of births, and family history of cancer, played key roles in gynecological (cervical, ovarian, endometrial) cancer risk due to exposure to ambient air pollution (NO_2, SO_2, and PM_{10}). These were the contributing factors used to identify the sensitive population who are more susceptible to the gynecological cancer risk attributable to air pollution exposure. In most of the included studies, the studies’ findings indicated that medium- and long-term exposure to ambient air pollutants played a vital role in gynecological cancer development. In most cases, the sensitivity analysis suggested that long-term exposure to air pollutants NO_2, SO_2, and PM_{10} had

varying impacts on different groups of women. Similarly, a study conducted in Changsha, China, suggested that women without a family history of cancer, women with low SES, women who had given birth and had more children, and women above 45 years of age were more susceptible to the gynecological cancer risk due to long term SO_2 exposure [60]. Other studies conducted in Beijing and abroad have shown almost similar findings [61-63,66].

In line with previous studies, the major setbacks while interpreting our study results and factors associated with the effect of exposure to ambient air pollution on gynecological cancer were the presence of other ambient air pollutants (SOx, $PM_{2.5}$, O_3, CO, and H_2S) and exposure bias. We speculated that ambient air pollution had associations with the gynecological cancer risk in women in China. The women's occupation, family history of cancer, age, number of births, and procreation were the major confounding factors that could be considered in the study. The other factors, for example, environmental tobacco smoke (ETS), drinking, and menstruation cycle showed no significant interaction between the risk of gynecological (cervical, ovarian, endometrial) cancer and ambient air pollution exposure.

Based on our analysis, women who had given birth and had more children, older women (⩾40 years), women with high SES, and women without a family history of cancer were more susceptible to the risk of medium- and long-term exposure to ambient NO_2, and long-term exposure to SO_2. This study met the objective of determining the associations between exposure to ambient air pollution (SO_2, PM_{10}, and NO_2) during the past 1 year, 5 years, 10 years, and 15 years on gynecological (ovarian, endometrial, and cervical) cancer and identifying the sensitive population who are more susceptible to the gynecological cancer risk due to air pollution exposure. While we speculate confounding factors that might give the heterogeneity on the effect of exposure to ambient air pollution on gynecological cancer, the analysis was accurate. Confounding predictors including occupation, age, procreation, a family history of cancer, and the number of births are important factors that determine gynecological cancer [60,65,77,78].

Similar association was observed in a recent case-control study conducted in a Changsha, China [60]. The participants were women aged between 10 years - 90 years. The exposure was focused on SO2, and was measured as the past 1 year, 5 years, 10 years to 15 years before the women were first diagnosed with gynecological (cervical, ovarian, endometrial) cancer. The study found positive associations between cancer and SO_2. The findings from the study were justifiable since there were similarities with the findings from the current study.

The comprehensive systematic review and meta-analysis we conducted is indeed a parameter to objectively access the factors related to air pollution and gynecological cancer risk among women globally. Our results provide scientific evidence to improve gynecological cancer screening services. Once the visits for gynecological check-ups are ascertained, the prevention of harm and disabilities resulting from gynecological cancer is ensured. This is achieved through voluntary gynecological cancer screening, which is considered as one of the most beneficial healthcare services for women. Furthermore, the number of gynecologic health centers and accessibility to them means a lot. The higher the number of gynecological healthcare screening facilities in society, the more optimal the visits are. The health of women usually corresponds to the health of society.

There was a higher number of gynecological cancer cases due to the higher concentration of atmospheric pollutants such as SO_2, NO_2, and PM_{10}, among others [63,64]. The notorious and lethal effects of air pollution served as a foundation to enlighten women toward participation in

gynecological cancer screening. This was also seen in the USA through similar studies that showed that women with low SES and childbearing age suffered more from gynecological cancer [61,62]. Additionally, a similar study in Saudi Arabia concluded that high levels of NO_2 can have a positive effect on cervical and ovarian cancer [67]. The findings from these studies suggest that alternatives for gynecological cancer screening should be prioritized to control cervical cancers [68]. In general, public health officials may promote interaction with gynecological health services to enable women to seek access to gynecological care services more efficiently. This means that the importance attached to gynecological care during a woman's life extends for a lifetime.

The discussions in our review were in line with those of a study conducted in the USA, which deduced that it is through HPV vaccination, testing, and Pap smear-based screening, that an environment that promotes women's gynecological health can be created [68,78]. Hence, regular gynecological cancer screening needs to be prioritized if gynecological cancers are to be controlled. In addition, it is essential to promote programs/policies and develop strategies for prevention, early detection, and interventions to effectively reduce air pollution and gynecological cancer risk. Finally, promoting participation in decision-making in matters pertaining to the gynecological health of women will boost their morals and the frequency of gynecological screening attendance.

Strength and Limitations

The study had two strengths: Firstly, a pre-specified protocol was used to search articles and extract data, and any possible assessor bias was lessened by the quality assessment of two independent investigators Secondly, sensitivity analysis was conducted to determine the robustness of the pooled estimate. The study had one limitation: The subgroup analysis showed no significant variation in heterogeneity compared to the overall result.

Implications of the Study

The more the exposure to air pollution, the more the gynecological cancer risk. Implications of these new findings suggest that susceptibility to gynecological cancer may result from long-term ambient air pollutants (NO_2 and SO_2) exposure at high concentrations, supporting the hypothesis that ambient air pollution may be associated with gynecological cancer. We considered trends in gynecological cancer incidence and deaths due to short- and long-term exposure to SO_2 and NO_2 in the previous case-control, cohort, and population-based studies and deduced that mortality rates increased with an increase in NO_2 and SO_2 levels due to air pollution.

Findings from the report should be used in future research on gynecological cancer and ambient air pollution. The findings can promote programs/policies and develop strategies for the prevention, early detection, and interventions to effectively reduce gynecological cancer risk and ambient air pollution in China. This will promote the delivery of important health services, such as gynecological cancer screening, gynecological cancer treatment, and gynecological health counseling. Furthermore, the results would support the need for a more detailed exposure assessment of exposure to atmospheric NO_2 and SO_2 in gynecological cancer development. However, the mode and study selection for this requires further research to ascertain the effectiveness of the intervention in China.

CONCLUSION

In regions where air pollution was high, there were increased gynecological cancer cases. This confers a vital effect of short- and long-term exposure to ambient air pollution on gynecological cancer. These findings support that exposure to ambient NO_2 for 5 years or longer and long-term exposure to ambient SO_2 for more than 15 years, at high concentrations, was significantly associated with gynecological (ovarian, endometrial, and cervical) cancers.

However, no significant association was observed for short-term exposure to air pollution.

Aside from high levels of atmospheric pollutants in most of our study settings, access to essential gynecological cancer screening is often overlooked. This is specifically for the less educated women, poorer women, and financial constraints. This situation will need to be addressed to ensure improved gynecological healthcare services to less privileged women. Although these barriers are similar across Asian countries, differences exist concerning the extent and nature of the problem. Hence, individual country-specific schemes are required to tackle the challenges raised.

ACKNOWLEDGMENTS

We would like to thank the authors and their colleagues who contributed to the availability of evidence needed to compile this article. We would also like to thank the reviewers for their very helpful and valuable comments and suggestions for improving the paper.

FUNDING

None.

AVAILABILITY OF DATA AND MATERIALS

Data are available upon request, please contact author for data requests.

DECLARATIONS

Ethics Approval and Consent to Participate

This review is exempt from ethics approval because we collected and synthesized data from previous epidemiological studies in which informed consent has already been obtained by the investigators.

Consent for Publication

All authors agreed to this publication.

Competing Interests

The authors declare that they have no competing interests.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, et al. (2018) Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians 68(6): 394-424.
2. La Rosa VL, Garzon S, Gullo G, et al. (2020a) Fertility preservation in women affected by gynaecological cancer: The importance of an integrated gynaecological and psychological approach. Ecancermedicalscience 14: 1035.
3. Muls A, Andreyev J, Lalondrelle S, et al. (2017) Systematic review: The impact of cancer treatment on the gut and vaginal microbiome in women with a gynecological malignancy. International Journal of Gynecologic Cancer 27(7): 1550-1559.
4. Lingeman CH (1983) Environmental factors in the etiology of carcinoma of the human ovary: A review. American Journal of Industrial Medicine 4(1-2): 365-379.
5. Liu J, Xu Z, Zhang K, et al. (2014) Characteristics of Malignant Tumors in 230 Husband–Wife Pairs. Cell Biochemistry and Biophysics 70: 123-127.
6. Fitzmaurice C, Abate D, Abbasi N, et al. (2019) Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: A systematic analysis for the global burden of disease study. JAMA Oncology 5(12): 1749-1768.
7. Amer MH (1982) Pattern of cancer in Saudi Arabia: A personal experience based on the management of 1000 patients. Part 1. Annals of Saudi Medicine 2(4): 203-213.

8. Zhao M, Gu L, Li Y, et al. (2019) Chitooligosaccharides display anti-tumor effects against human cervical cancer cells via the apoptotic and autophagic pathways. Carbohydrate Polymers 224: 115171.
9. Ferlay J, Soerjomataram I, Dikshit R, et al. (2015) Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer 136(5): E359-E386.
10. Cancer-Cervix (2019) IAfRo. Cancer fact sheets: Cervical cancer.
11. Cancer-Corpus (2019) IAfRo. Cancer fact sheets: Corpus Cancer.
12. cancer-Ovary (2019) IAfRo. Cancer fact sheets: Ovary Cancer.
13. de Melo AS, de Paula CTV, Rufato MAF, et al. (2019) Fertility optimization in women with cancer: From preservation to contraception. JBRA Assisted Reproduction 23(4): 418-429.
14. Chen W, Zheng R, Zeng H, et al. (2016) The incidence and mortality of major cancers in China, 2012. Cancer Communications 35(1): 1-5.
15. McKenzie ND, Kennard JA, Ahmad S (2018) Fertility preserving options for gynecologic malignancies: A review of current understanding and future directions. Critical Reviews in Oncology/Hematology 132: 116-124.
16. Carré J, Gatimel N, Moreau J, et al. (2017) Does air pollution play a role in infertility?: A systematic review. Environmental Health 16: 1-16.
17. Salani R, Billingsley CC, Crafton SM (2014) Cancer and pregnancy: An overview for obstetricians and gynecologists. American Journal of Obstetrics and Gynecology 211(1): 7-14.
18. Huffman LB, Hartenbach EM, Carter J, et al. (2016) Maintaining sexual health throughout gynecologic cancer survivorship: A comprehensive review and clinical guide. Gynecologic Oncology 140(2): 359-368.
19. Shankar A, Prasad N, Roy S, et al. (2017) Sexual dysfunction in females after cancer treatment: An unresolved issue. Asian Pacific Journal of Cancer Prevention: APJCP 18(5): 1177-1182.
20. Vermeer WM, Bakker RM, Kenter GG, et al. (2016) Cervical cancer survivors' and partners' experiences with sexual dysfunction and psychosexual support. Supportive Care in Cancer 24: 1679-1687.
21. Carter J, Stabile C, Gunn A, et al. (2013) The physical consequences of gynecologic cancer surgery and their impact on sexual, emotional, and quality of life issues. The Journal of Sexual Medicine 10(Supplement_1): 21-34.
22. Iżycki D, Woźniak K, Iżycka N (2016) Consequences of gynecological cancer in patients and their partners from the sexual and psychological perspective. Menopause Review/Przegląd Menopauzalny 15(2): 112-116.
23. La Rosa VL, Shah M, Kahramanoglu I, et al. (2020) Quality of life and fertility preservation counseling for women with gynecological cancer: An integrated psychological and clinical perspective. Journal of Psychosomatic Obstetrics & Gynecology 41(2): 86-92.
24. Holnicki P, Tainio M, Kałuszko A, et al. (2017) Burden of mortality and disease attributable to multiple air pollutants in Warsaw, Poland. International Journal of Environmental Research and Public Health 14(11): 1359.
25. Su SY, Liaw YP, Jhuang JR, et al. (2019) Associations between ambient air pollution and cancer incidence in Taiwan: An ecological study of geographical variations. BMC Public Health 19: 1-8.
26. Manisalidis I, Stavropoulou E, Stavropoulos A, et al. (2020) Environmental and health impacts of air pollution: A review. Frontiers in Public Health 8: 14.
27. Huang YB, Song FJ, Liu Q, et al. (2014) A bird's eye view of the air pollution-cancer link in China. Chinese Journal of Cancer 33(4): 176.

28. Bray F, Ferlay J, Laversanne M, et al. (2015) Cancer incidence in five continents: Inclusion criteria, highlights from Volume X and the global status of cancer registration. International Journal of Cancer 137(9): 2060-2071.
29. Ginsburg O, Bray F, Coleman MP, et al. (2017) The global burden of women's cancers: A grand challenge in global health. The Lancet 389(10071): 847-860.
30. Habib SH, Saha S (2010) Burden of non-communicable disease: Global overview. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 4(1): 41-47.
31. Yu Q, Zhang L, Hou K, et al. (2021) Relationship between air pollutant exposure and gynecologic cancer risk. International Journal of Environmental Research and Public Health 18(10): 5353.
32. Hung LJ, Chan TF, Wu CH, et al. (2012) Traffic air pollution and risk of death from ovarian cancer in Taiwan: Fine particulate matter (PM2. 5) as a proxy marker. Journal of Toxicology and Environmental Health, Part A 75(3): 174-182.
33. Li X, Ding L, Song L, et al. (2020) Effects of exposure to polycyclic aromatic hydrocarbons combined with high-risk human papillomavirus infection on cervical intraepithelial neoplasia: A population study in Shanxi Province, China. International Journal of Cancer 146(9): 2406-2412.
34. Scheurer ME, Danysh HE, Follen M, et al. (2014) Association of traffic-related hazardous air pollutants and cervical dysplasia in an urban multiethnic population: A cross-sectional study. Environmental Health 13: 1-8.
35. Brody JG, Moysich KB, Humblet O, et al. (2007) Environmental pollutants and breast cancer: Epidemiologic studies. Cancer: Interdisciplinary International Journal of the American Cancer Society 109: 2667-2711.
36. Hombach-Klonisch S, Pocar P, Kietz S, et al. (2005) Molecular actions of polyhalogenated arylhydrocarbons (PAHs) in female reproduction. Current Medicinal Chemistry 12(5): 599-616.
37. García-Pérez J, Lope V, López-Abente G, et al. (2015) Ovarian cancer mortality and industrial pollution. Environmental Pollution 205: 103-110.
38. Liu T, Song Y, Chen R, et al. (2020) Solid fuel use for heating and risks of breast and cervical cancer mortality in China. Environmental Research 186: 109578.
39. Young MT, Sandler DP, DeRoo LA, et al. (2014) Ambient air pollution exposure and incident adult asthma in a nationwide cohort of US women. American Journal of Respiratory and Critical Care Medicine 190(8): 914-921.
40. Brook RD, Rajagopalan S, Pope III CA, et al. (2010) Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation 121(21): 2331-2378.
41. Chen H, Kwong JC, Copes R, et al. (2017) Living near major roads and the incidence of dementia, Parkinson's disease, and multiple sclerosis: A population-based cohort study. The Lancet 389(10070): 718-726.
42. Bowe B, Xie Y, Li T, et al. (2018) Particulate matter air pollution and the risk of incident CKD and progression to ESRD. Journal of the American Society of Nephrology 29(1): 218-230.
43. Hamra GB, Laden F, Cohen AJ, et al. (2015) Lung cancer and exposure to nitrogen dioxide and traffic: A systematic review and meta-analysis. Environmental Health Perspectives 123(11): 1107-1112.
44. Andersen ZJ, Stafoggia M, Weinmayr G, et al. (2017) Long-term exposure to ambient air pollution and incidence of postmenopausal breast cancer in 15 European cohorts within the ESCAPE project. Environmental Health Perspectives 125(10): 107005.
45. Turner MC, Andersen ZJ, Baccarelli A, et al. (2020) Outdoor air pollution and cancer: An overview of the current evidence and public health recommendations. CA: A Cancer Journal for Clinicians 70(6): 460-479.

46. McKean-Cowdin R, Calle EE, Peters JM, et al. (2009) Ambient air pollution and brain cancer mortality. Cancer Causes & Control 20: 1645-1651.
47. Ancona C, Badaloni C, Mataloni F, et al. (2015) Mortality and morbidity in a population exposed to multiple sources of air pollution: A retrospective cohort study using air dispersion models. Environmental Research 137: 467-474.
48. Nagel G, Stafoggia M, Pedersen M, et al. (2018) Air pollution and incidence of cancers of the stomach and the upper aerodigestive tract in the European Study of Cohorts for Air Pollution Effects (ESCAPE). International Journal of Cancer 143(7): 1632-1643.
49. Lavigne É, Bélair MA, Do MT, et al. (2017) Maternal exposure to ambient air pollution and risk of early childhood cancers: a population-based study in Ontario, Canada. Environment International 100: 139-147.
50. Boffetta P, Dosemeci M, Gridley G, et al. (2001) Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women. Cancer Causes & Control 12: 365-374.
51. Guo J, Kauppinen T, Kyyrönen P, et al. (2004) Risk of esophageal, ovarian, testicular, kidney and bladder cancers and leukemia among Finnish workers exposed to diesel or gasoline engine exhaust. International Journal of Cancer 111(2): 286-292.
52. Iwai K, Mizuno S, Miyasaka Y, et al. (2005) Correlation between suspended particles in the environmental air and causes of disease among inhabitants: Cross-sectional studies using the vital statistics and air pollution data in Japan. Environmental Research 99(1): 106-117.
53. Sharma A, Verma HK, Joshi S, et al. (2015) A link between cold environment and cancer. Tumor Biology 36: 5953-5964.
54. Chen G, Wan X, Yang G, et al. (2015) Traffic-related air pollution and lung cancer: A meta-analysis. Thoracic Cancer 6(3): 307-318.
55. Miao Y, Shen YM, Lu C, et al. (2017) Maternal exposure to ambient air temperature during pregnancy and early childhood pneumonia. Journal of Thermal Biology 69: 288-293.
56. Brown CA, Sohani SB, Khan K, et al. (2008) Antenatal care and perinatal outcomes in Kwale district, Kenya. BMC Pregnancy and Childbirth 8: 1-11.
57. Neyeloff JL, Fuchs SC, Moreira LB (2012) Meta-analyses and Forest plots using a microsoft excel spreadsheet: Step-by-step guide focusing on descriptive data analysis. BMC Research Notes 5: 1-6.
58. Munn Z, Moola S, Lisy K, et al. (2015) Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. JBI Evidence Implementation 13(3): 147-153.
59. Xu Q, Lu C, Murithi RG, et al. (2022) Increase associated risk of gynaecological cancer due to long-term exposure to high concentration of atmospheric SO2 industrial pollutant. Indoor and Built Environment 31(8): 2183-2192.
60. Villanueva C, Chang J, Ziogas A, et al. (2021) Ambient air pollution and ovarian cancer survival in California. Gynecologic Oncology 163(1): 155-161.
61. Ayuso-Álvarez A, García-Pérez J, Triviño-Juárez JM, et al. (2020) Association between proximity to industrial chemical installations and cancer mortality in Spain. Environmental Pollution 260: 113869.
62. Shi JF, Canfell K, Lew JB, et al. (2012) The burden of cervical cancer in China: synthesis of the evidence. International Journal of Cancer 130(3): 641-652.
63. Wu J, Sun H, Yang L, et al. (2018) Improved survival in ovarian cancer, with widening survival gaps of races and socioeconomic status: A period analysis, 1983-2012. Journal of Cancer 9(19): 3548.

64. Al-Ahmadi K, Al-Zahrani A (2013) NO2 and cancer incidence in Saudi Arabia. International Journal of Environmental Research and Public Health 10(11): 5844-5862.
65. Adegoke O, Kulasingam S, Virnig B (2012) Cervical cancer trends in the United States: A 35-year population-based analysis. Journal of Women's Health 21(10): 1031-1037.
66. Lai JCY, Weng CS, Huang SM, et al. (2017) Incidence and lifetime risk of uterine corpus cancer in Taiwanese women from 1991 to 2010. Taiwanese Journal of Obstetrics and Gynecology 56(1): 68-72.
67. Matz M, Coleman MP, Carreira H, et al. (2017) Worldwide comparison of ovarian cancer survival: Histological group and stage at diagnosis (CONCORD-2). Gynecologic Oncology 144(2): 396-404.
68. Jiang X, Tang H, Chen T (2018) Epidemiology of gynecologic cancers in China. Journal of Gynecologic Oncology 29(1): e7.
69. Chen W, Sun K, Zheng R, et al. (2018) Cancer incidence and mortality in China, 2014. Chinese Journal of Cancer Research 30(1): 1-12.
70. Vieira VM, Villanueva C, Chang J, et al. (2017) Impact of community disadvantage and air pollution burden on geographic disparities of ovarian cancer survival in California. Environmental Research 156: 388-393.
71. Chen TC, Lee JY, Wang SY, et al. (2005) Relevant factors for cervical cancer among young women in Taiwan. Taiwanese Journal of Obstetrics and Gynecology 44(2): 143-147.
72. Mukerjee D (2015) Impact of environment pollution on cancer mortality in India and possible preventive measures to reduce the risk. SMU Medicine 2(1): 253-269.
73. Clapp R (2000) Environment and health: 4. Cancer. CMAJ, 163(8): 1009-1012.
74. Karoutsou E, Karoutsos P, Karoutsos D (2016) Adverse effects on female human reproductive health from exposure to endocrine disruptors: Focus on endometrial lesions. Journal of Clinical Epigenetics 2(4).
75. Boyle P, Leon ME, Maisonneuve P, et al. (2003) Cancer control in women. Update 2003. International Journal of Gynecology & Obstetrics 83: 179-202.
76. Friedlander M, de Souza P, Segelov E (1992) Risk factors, epidemiology, screening, and prognostic factors in female genital cancer. Current Opinion in Oncology 4(5): 913-922.
77. Wang T, Townsend MK, Simmons V, et al. (2020) Prediagnosis and postdiagnosis smoking and survival following diagnosis with ovarian cancer. International Journal of Cancer 147(3): 736-746.
78. Kinde I, Bettegowda C, Wang Y, et al. (2013) Evaluation of DNA from the Papanicolaou test to detect ovarian and endometrial cancers. Science Translational Medicine 5(167): 167ra4-167ra4.